



Inventors: Gurney et al.
Title: "Alzheimer's Disease Secretase, APP Substrates
Therefor, and Uses Therefor"
Atty. Ref.: 29915/6280NCP
Phone No.: (312) 474-6300

Fig. 1A
1/18

FIGURE 1A

ATGGGCGCACTGGCCCAGGGCGCTGCTGCTGCCCTGCTGGCCCAGTGGCTCCTGCGCGCC
M G A L A R A L L P L L A Q W L L R A
CCCCGGAGCTGGCCCCCGGCCCTCACGCTGCCCTCCGGTGGCCGGCACGAAC
A P E L A P A P F T L P L R V A A A A T N
CGCGTAGTTGCGCCCACCCCGGGACCCGGGACCCCTGCCGAGCGCCACGCCGACGGCTTG
R V V A P T P G P G T P A E R H A D G L
GCGCTGCCCTGGAGCCTGCCCTGGCGTCCCCCGCGGGCGCCAACTTCTGGCCATG
A L A L E P A L A S P A G A A A N F L A M
GTAGACAAACCTGCAGGGGACTCTGGCCCGGCTACTACCTGGAGATGCTGATCGGGACC
V D N L Q G D S G R G Y Y L E M L I G T
CCCCCGCAGAAGCTACAGATTCTCGTTGACACTGGAAGCAGTAACCTTGCCGTGGCAGGA
P P Q K L Q I L V D T G S S N F A V A G
ACCCCGCACTCCTACATAGACACGTACTTGACACAGAGAGGTCTAGCACATACCGCTCC
T P H S Y I D T Y F D T E R S S T Y R S
AAGGGCTTGACGTACAGTGAAGTACACACAAGGAAGCTGGACGGGCTTCGTTGGGAA
K G F D V T V K Y T Q G S W T G F V G E
GACCTCGTACCATCCCCAAAGGCTTCATAACTTCTTTCTTGTCAACATTGCCACTATT
D L V T I P K G F N T S F L V N I A T I
TTTGAATCAGAGAATTCTTTCTGGCTGGATTAAATGGAATGGAATACTTGGCCTAGCT
F E S E N F F L P G I K W N G I L G L A
TATGCCACACTTGCCAAGCCATCAAGTTCTCTGGAGACCTTCTCGACTCCCTGGTGACA
Y A T L A K P S S S L E T F F D S L V T
CAAGCAAACATCCCCAACGTTTCTCCATGCAGATGTGTGGAGGCCGGCTGCCGTTGCT
Q A N I P N V F S M Q M C G A G L P V A
GGATCTGGGACCAACGGAGGTAGTCTTGTCTGGTGGAAATTGAACCAAGTTGTATAAA
G S G T N G G S L V L G G I E P S L Y K
GGAGACATCTGGTATAACCCCTATTAAGGAAGAGTGGTACTACCAGATAGAAATTCTGAAA
G D I W Y T P I K E E W Y Y Q I E I L K
TTGGAAATTGGAGGCCAAAGCCTTAATCTGGACTGCAGAGAGTATAACGCAGACAAGGCC
L E I G G Q S L N L D C R E Y N A D K A
ATCGTGGACAGTGGCACCAACGCTGCTGCCCTGCCCCAGAAGGTGTTGATCGGGTGGTG
I V D S G T T L L R L P Q K V F D A V V
GAAGCTGTGGCCCGCGCATCTCTGATTCCAGAATTCTCTGATGGTTCTGGACTGGTCC
E A V A R A S L I P E F S D G F W T G S
CAGCTGGCGTGGACGAATTGGAAACACCTGGTCTTACTTCCCTAAAATCTCCATC
Q L A C W T N S E T P W S Y F P K I S I
TACCTGAGAGATGAGAACTCCAGCAGGTCAATTCCGTATCACAATCCTGCCAGCTTAC
Y L R D E N S S R S F R I T I L P Q L Y
ATTCAAGCCCATGATGGGGCCGGCCTGAATTATGAATGTTACCGATTGGCATTCCCCA
I Q P M M G A G L N Y E C Y R F G I S P

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Fig. 1B

Phone No.: (312) 474-6300

2/18

FIGURE 1B

TCCACAAATGCGCTGGTATCGGTGCCACGGTATGGAGGGCTTCTACGTATCTCGAC
S T N A L V I G A T V M E G F Y V I F D
AGAGCCCAGAAGAGGGTGGGCTTCGAGCGAGCCCTGTGCAGAAATTGCAGGTGCTGCA
R A Q K R V G F A A S P C A E I A G A A
GTGTCTGAAATTTCGGGCCTTCTAACAGAGGATGTAGCCAGCAACTGTGTCCCCGCT
V S E I S G P F S T E D V A S N C V P A
CAGTCTTGAGCGAGCCCATTGTGGATTGTGTCCTATGCGCTCATGAGCGTCTGTGGA
Q S L S E P I L W I V S Y A L M S V C G
GCCATCCTCCTGTCTTAATCGTCCTGCTGCTGCCGTTCCGGTGTCAAGCGTCGCCCC
A I L L V L I V L L L P F R C Q R R P
CGTGACCTGAGGTCGTCAATGATGAGTCCTCTGGTCAGACATCGCTGGAAATGAATA
R D P E V V N D E S S L V R H R W K

GCCAGGCCTGACCTCAAGCAACCCTGAACCTCAGCTATTAAGAAAATCACATTCCAGGGC
AGCAGCCGGATCGATGGTGGCGCTTCTCCTGTGCCACCCGTCTCAATCTCTGTTCT
GCTCCCAGATGCCTCTAGATTCACTGTCTTGATTTCAGCTTCAAACGCTTCAAATC
CTCCCTACTTCCAAGAAAAATAATTAAAAAAACTTCATTCTAAACCAAAAAAA
AAAA

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Fig. 2A

3/18

FIGURE 2A

ATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGGCGCGGGAGTGCTGCCTGCCAC
M A Q A L P W L L L W M G A G V L P A H
GGCACCCAGCACGGCATCCGGCTGCCCTGCGCAGCGCCTGGGGGGCGCCCCCTGGGG
G T Q H G I R L P L R S G L G G A P L G
CTGCGGCTGCCCGGGAGACCGACGAAGAGCCCAGGGAGGCCGGCCGGAGGGCAGCTTT
L R L P R E T D E E P E E P G R R G S F
GTGGAGATGGTGGACAACCTGAGGGCAAGTCGGGCAGGGCTACTACGTGGAGATGACC
V E M V D N L R G K S G Q G Y Y V E M T
GTGGGCAGCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTTGCA
V G S P P Q T L N I L V D T G S S N F A
GTGGGTGCTGCCCTTACCCCTTCATCGCTACTACCAGAGGCAGCTGTCCAGCACA
V G A A P H P F L H R Y Y Q R Q L S S T
TACCGGGACCTCCCGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAG
Y R D L R K G V Y V P Y T Q G K W E G E
CTGGGCACCGACCTGGTAAGCATCCCCATGGCCCAACGTCACTGTGCGTGCACACATT
L G T D L V S I P H G P N V T V R A N I
GCTGCCATCACTGAATCAGACAAGTTCTCATCAACGGCTCCAACGGAAAGGCATCCTG
A A I T E S D K F F I N G S N W E G I L
GGGCTGGCCTATGCTGAGATTGCCAGGCTTGTGGTGGCTGGCTCCCCCTCAACCGAGTCT
G L A Y A E I A R L C G A G F P L N Q S
GAAAGTGGCTGGCCTCTGTCGGAGGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTAC
E V L A S V G G S M I I G G I D H S L Y
ACAGGCAGTCTCTGGTATACACCCATCCGGGGAGTGGTATTATGAGGTGATCATTGTG
T G S L W Y T P I R R E W Y Y E V I I V
CGGGTGGAGATCAATGGACAGGATCTGAAATGGACTGCAAGGAGTACAACATGACAAG
R V E I N G Q D L K M D C K E Y N Y D K
AGCATTGGACAGTGGCACCAACCTCGTTGCCAAGAAAGTGGTGAAGCTGCA
S I V D S G T T N L R L P K K V F E A A
GTCAAATCCATCAAGGCAGCCTCCACGGAGAAGTCCCTGATGGTTCTGGCTAGGA
V K S I K A A S S T E K F P D G F W L G
GAGCAGCTGGTGTGGCAAGCAGGCACCACCCCTGGAACATTTCAGTCATCTCA
E Q L V C W Q A G T T P W N I F P V I S
CTCTACCTAATGGGTGAGGTTACCAACCAGTCCTCCGCATCACCACCTCCGCAGCAA
L Y L M G E V T N Q S F R I T I L P Q Q
TACCTGCGGCCAGTGGAGATGTGGCCACGTCCCAAGACGACTGTTACAAGTGGTGCATC
Y L R P V E D V A T S Q D D C Y K F A I
TCACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAGGGCTTCTACGTTGTC
S Q S S T G T V M G A V I M E G F Y V V
TTTGATGGGCCGAAACGAATTGGCTTGCTGTCAGCGCTGCCATGTGCACGATGAG
F D R A R K R I G F A V S A C H V H D E

FIGURE 2B

TTCAGGACGGCAGCGGTGGAAGGCCCTTGTACCTGGACATGGAAGACTGTGGCTAC
F R T A A V E G P F V T L D M E D C G Y
AACATTCCACAGACAGATGAGTCAACCCTCATGACCATAGCCTATGTCATGGCTGCCATC
N I P Q T D E S T L M T I A Y V M A A I
TGCGCCCTCTTCATGCTGCCACTCTGCCTCATGGTGTGTCAGTGGCGCTGCCTCCGCTGC
C A L F M L P L C L M V C Q W R C L R C
CTGCGCCAGCAGCATGATGACTTGCTGATGACATCTCCCTGCTGAAGTGAGGAGGCCA
L R Q Q H D D F A D D I S L L K

TGGGCAGAAGATAGAGATTCCCTGGACACACCTCCGTGGTCACTTGGTCACAAGTA
GGAGACACAGATGGCACCTGTGGCCAGAGCACCTCAGGACCCCTCCCCACCCACCAAATGC
CTCTGCCTTGATGGAGAAGGAAAAGGCTGGCAAGGTGGTCCAGGGACTGTACCTGTAG
GAAACAGAAAAGAGAAGAAAGAAGCAGTCTGCTGGCGGGAAATACTCTTGGTCACCTCAAA
TTAAGTCGGAAATTCTGCTGCTGAAACTTCAGCCCTGAACCTTGTCCACCATTCC
TTAAATTCTCAACCCAAAGTATTCTCTTCTTAGTTCTAGAAGTACTGGCATCACAC
GCAGGTTACCTTGGCGTGTGCCCTGTGGTACCCCTGGCAGAGAAGAGACCAAGCTGTT
CCCTGCTGCCAAAGTCAGTAGGAGAGGATGCACAGTTGCTATTGCTTAGAGACAGG
GACTGTATAAACACAAGCCTAACATTGGTGAAAGATTGCCTCTTGAAAAA

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Fig. 3A

5/18

FIGURE 3A

ATGGCCCAAGCCCTGCCCTGGCTCCTGCTGTGGATGGCGCGGGAGTGCTGCCTGCCAC
M A Q A L P W L L L W M G A G V L P A H
GGCACCCAGCACGGCATCCGGCTGCCCTGCGCAGCGCCTGGGGGGCGCCCCCTGGGG
G T Q H G I R L P L R S G L G G A P L G
CTGCGGCTGCCCGGGAGACCGACGAAGAGCCCAGGGAGGCCGGCCGGAGGGCAGCTTT
L R L P R E T D E E P E E P G R R G S F
GTGGAGATGGTGGACAACCTGAGGGCAAGTCGGGCAGGGCTACTACGTGGAGATGACC
V E M V D N L R G K S G Q G Y Y V E M T
GTGGGCAGCCCCCGCAGACGCTCAACATCCTGGTGGATACAGGCAGCAGTAACTTGCA
V G S P P Q T L N I L V D T G S S N F A
GTGGGTGCTGCCCTCACCCCTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACA
V G A A P H P F L H R Y Y Q R Q L S S T
TACCGGGACCTCCGGAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAG
Y R D L R K G V Y V P Y T Q G K W E G E
CTGGGCACCGACCTGGTAAGCATCCCCATGGCCCCAACGTCACTGTGCGTGCCAACATT
L G T D L V S I P H G P N V T V R A N I
GCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCCAACGGAAAGGCATCCTG
A A I T E S D K F F I N G S N W E G I L
GGGCTGGCCTATGCTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTCTTGACTCT
G L A Y A E I A R P D D S L E P F F D S
CTGGTAAAGCAGACCCACGTTCCAACCTCTCCCTGCAGCTTGTGGTGGCTTC
L V K Q T H V P N L F S L Q L C G A G F
CCCTCAACCAGTCTGAAGTGCTGGCCTCTGCGGAGGCATGATCATGGAGGTATC
P L N Q S E V L A S V G G S M I I G G I
GACCACTCGCTGTACACAGGCAGTCTGGTATAACACCCATCCGGCGGGAGTGGTATTAT
D H S L Y T G S L W Y T P I R R E W Y Y
GAGGTCATCATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAAATGGACTGCAAGGAG
E V I I V R V E I N G Q D L K M D C K E
TACAACATATGACAAGAGCATTGTGGACAGTGGCACCACCAACCTCGTTGCCAAGAAA
Y N Y D K S I V D S G T T N L R L P K K
GTGTTTGAAGCTGCAGTCAAATCCATCAAGGCAGCCTCCACGGAGAAGTTCCCTGAT
V F E A A V K S I K A A S S T E K F P D
GGTTTCTGGCTAGGAGAGCAGCTGGTGTGGCAAGCAGGCACCAACCCCTGGAACATT
G F W L G E Q L V C W Q A G T T P W N I
TTCCCAGTCATCTCACTCTACCTAACCTAACGGTGGAGGTTACCAACCAGTCCTCCGCATCACC
F P V I S L Y L M G E V T N Q S F R I T
ATCCTTCCGCAGCAATACCTGCGGCCAGTGGAAAGATGTGGCCACGTCCCAAGACGACTGT
I L P Q Q Y L R P V E D V A T S Q D D C
TACAAGTTGCCATCTCACAGTCATCCACGGCACTGTTATGGGAGCTGTTATCATGGAG
Y K F A I S Q S S T G T V M G A V I M E

FIGURE 3B

GGCTTCTACGTTGCTTGATCGGGCCGAAAACGAATTGGCTTGCTGTCAGCGCTTGC
G F Y V V F D R A R K R I G F A V S A C
CATGTGCACGATGAGTCAGGACGGCAGCGGTGGAAGGCCCTTGTACCTGGACATG
H V H D E F R T A A V E G P F V T L D M
GAAGACTGTGGCTACAAACATTCCACAGACAGATGAGTCACCCCTCATGACCATA
GCTATGGCTGCCATCTGCCCTCTCATGCTGCCACTCTGCCATGGTGTGTCAGTGG
E D C G Y N I P Q T D E S T L M T I A Y
V M A A I C A L F M L P L C L M V C Q W
CGCTGCCTCCGCTGCCCTGCCAGCAGCATGATGACTTTGCTGATGACATCTCCCTGCTG
R C L R C L R Q Q H D D F A D D I S L L
AAGTGAGGAGGCCATGGCAGAAGATAGAGATTCCCTGGACCACACCTCCGTGGTCA
K

CTTGGTCACAAGTAGGAGACACAGATGGCACCTGTGGCCAGAGCACCTCAGGACCCCTCC
CCACCCACCAAATGCCTCTGCCCTGATGGAGAAGGAAAGGCTGGCAAGGTGGTTCCAG
GGACTGTACCTGTAGGAAACAGAAAAGAGAAGAAAGAAGCACTCTGCTGGCGGGAAACT
CTTGGTCACCTCAAATTAAAGTCGGAAATTCTGCTGCTGAAACTTCAGCCCTGAACCT
TTGTCCACCATTCCCTTAAATTCTCCAACCCAAAGTATTCTTCTTTCTTAGTTCAGAA
GTACTGGCATCACACGCAGGTTACCTTGGCGTGTGTCCTGTGGTACCCCTGGCAGAGAAG
AGACCAAGCTTGTTCCTGCTGGCAAAGTCAGTAGGAGAGGATGCACAGTTGCTATT
TGCTTAGAGACAGGGACTGTATAAACAAAGCTAACATTGGTGCAAAGATTGCCTCTTGA
ATTAAAAAAAAAAAAAAAAAAAAAA

FIGURE 4

ATGGCCCCAGCGCTGCACTGGCTCCTGCTATGGGGGGCTGGGAATGCTGCCTGCCAG
M A P A L H W L L W V G S G M L P A Q
GGAACCCATCTCGGCATCCGGCTGCCCTTCGCAGCGGCCTGGCAGGGCCACCCCTGGC
G T H L G I R L P L R S G L A G P P L G
CTGAGGCTGCCCGGGAGACTGACGAGGAATCGGAGGAGCCTGGCCGGAGAGGCAGCTT
L R L P R E T D E E S E E P G R R G S F
GTGGAGATGGTGGACAACCTGAGGGAAAGTCCGGCCAGGGCTACTATGTGGAGATGACC
V E M V D N L R G K S G Q G Y Y V E M T
GTAGGCAGCCCCCACAGACGCTCAACATCCTGGTGGACACGGGAGTAGTAACTTGCA
V G S P P Q T L N I L V D T G S S N F A
GTGGGGCTGCCACACCCTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACA
V G A A P H P F L H R Y Y Q R Q L S S T
TATCGAGACCTCCGAAAGGGTGTGTATGTGCCCTACACCCAGGGCAAGTGGGAGGGGAA
Y R D L R K G V Y V P Y T Q G K W E G E
CTGGGCACCGACCTGGTGGACATCCCTCATGGCCCCAACGTCACTGTGCGTGCCAACATT
L G T D L V S I P H G P N V T V R A N I
GCTGCCATCACTGAATCGGACAAGTTCTCATCAATGGTCCAACGGGAGGGCATCTA
A A I T E S D K F F I N G S N W E G I L
GGGCTGGCCTATGCTGAGATTGCCAGGCCGACGACTCTTGGAGCCCTTCTTGACTCC
G L A Y A E I A R P D D S L E P F F D S
CTGGTGAAGCAGACCCACATTCCAACATCTTCCCTGCAGCTCTGTGGCGCTGGCTTC
L V K Q T H I P N I F S L Q L C G A G F
CCCCTCAACCAGACCGAGGCACTGGCCTCGGTGGAGGGAGCATGATCATTGGTGGTATC
P L N Q T E A L A S V G G S M I I G G I
GACCACTCGTATACACGGCAGTCTCTGGTACACACCCATCCGGGGAGTGGTATTAT
D H S L Y T G S L W Y T P I R R E W Y Y
GAAGTGTACATTGTACGTGTGGAAATCAATGGTCAAGATCTCAAGATGGACTGCAAGGAG
E V I I V R V E I N G Q D L K M D C K E
TACAACCTACGACAAGAGCATTGGACAGTGGGACCAACCTTCGCTTGCCAAAGAAA
Y N Y D K S I V D S G T T N L R L P K K
GTATTGAAAGCTGCCGTCAAGTCCATCAAGGAGCCTCCGACGGAGAAGTCCCGGAT
V F E A A V K S I K A A S S T E K F P D
GGCTTTGGCTAGGGGAGCAGCTGGTGTGGCAAGCAGGACAGACCCCTGGAACATT
G F W L G E Q L V C W Q A G T T P W N I
TTCCCACTGATTTACCTCATGGTGAAGTCACCAATCAGTCCTCCGCATCACC
F P V I S L Y L M G E V T N Q S F R I T
ATCCCTCCTCAGCAATACCTACGGCCGGTGGAGGACGTGGCACGTCCAAAGACGACTGT
I L P Q Q Y L R P V E D V A T S Q D D C
TACAAGTTGCTGTCTCACAGTCATCCACGGGCACTGTTATGGGAGCCGTATCATGGAA
Y K F A V S Q S S T G T V M G A V I M E
GGTTTCTATGTCGTCCTCGATCGAGCCGAAAGCGAATTGGCTTGCTGTCAAGCGCTTGC
G F Y V V F D R A R K R I G F A V S A C
CATGTGCACGATGAGTTCAAGGACGGCGGAGTGGAAAGGTCCGTTACGGCAGACATG
H V H D E F R T A A V E G P F V T A D M
GAAGACTGTGGCTACAACATTCCCCAGACAGATGAGTCACACTATGACCATAGCCTAT
E D C G Y N I P Q T D E S T L M T I A Y
GTCACTGGCGGCCATCTGCCTGCCTCATGTTGCCACTCTGCCTCATGGTATGTCACTGG
V M A A I C A L F M L P L C L M V C Q W
CGCTGCCTGCCTGCCTGCCTGCCACCGACGATGACTTTGCTGATGACATCTCCCTGCTC
R C L R C L R H Q H D D F A D D I S L L
AAGTAAGGAGGCTGTGGCAGATGATGGAGACGCCCTGGACCACATCTGGTGGTCC
K
CTTGGTCACATGAGTTGGAGCTATGGATGGTACCTGTGGCAGAGCACCCTCAGGACCC
CACCAACCTGCCAATGCTTCTGGCGTACAGAACAGAGAAATCAGGCAAGCTGGATTACA
GGGCTTGACCTGTAGGACACAGGAGAGGGAGGAAGCAGCGCTCTGGTGGCAGGAATAT
CCTTAGGCACCAACAAACTTGAGTTGGAAATTGCTGCTGAGCTTCAGCCCTGACCC
CTGCCAGCATCTTCTAGAGTCCTAACCTAAAGTATTCTTATGTCCTTCCAGAAGTAC
TGGCGTCAACTCAGGCTACCCGGCATGTGTCCCTGTGGTACCCCTGGCAGAGAAAGGGC
AATCTCATTCCCTGCTGGCCAAGTCAGCAGAAGAAGGTGAAGTTGCCAGTTGCTT
TGATAGGAGTGCAGACTCAAGCCTACACTGGTACAAAGACTGCGTCTGAGATAACAA
GAA

FIGURE 5

1 MAQALPWLLLWMGAGVLPAGHTQHGIRLPLRSGLGGAPLGLRLPRETDEE 50
1 MAPALHWLLLWVGSGMLPAQGTHLGIRLPLRSGLAGPPLGLRLPRETDEE 50
51 PEEPGRGGSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFA 100
151 SEEPGRGGSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFA 100
101 VGAAPHFLHRYYQRQLSSTYRDLRKGVYVPTYQGKWEGETGDLVSI 150
101 VGAAPHFLHRYYQRQLSSTYRDLRKGVYVPTYQGKWEGETGDLVSI 150
151 GPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFDS 200
151 GPNVTVRANIAAITESDKFFINGSNWEGILGLAYAEIARPDDSLEPFDS 200
201 LVKQTHVPNLFSLQLCGAGFPLNQSEVLASVGGSMIIGGIDHSLYTGSLW 250
201 LVKQTHIPNIFSLQLCGAGFPLNQTEALASVGGSMIIGGIDHSLYTGSLW 250
251 YTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKK 300
251 YTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKK 300
301 VFEAAVKSIAASSTEKFPDGFWLGEQLVCWQAGTPWNIFPVISLYLMG 350
301 VFEAAVKSIAASSTEKFPDGFWLGEQLVCWQAGTPWNIFPVISLYLMG 350
351 EVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME 400
351 EVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAVSQSSTGTVMGAVIME 400
401 GFYVVFDRAKRIGFAVSACHVHDEFRTAAVEGPFTLDMEDCGYNIPQT 450
401 GFYVVFDRAKRIGFAVSACHVHDEFRTAAVEGPFTADMEDCGYNIPQT 450
451 DESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRQQHDDFADDISLL 500
451 DESTLMTIAYVMAAICALFMLPLCLMVCQWRCLRCLRHQQHDDFADDISLL 500
501 K 501
501 K 501

FIGURE 6A

ATGGCTAGCATGACTGGTGGACAGCAAATGGGTCGCAGATCCACCCAGCACGGCATCCGG
M A S M T G G Q Q M G R G S T Q H G I R
CTGCCCCCTGCGCAGCGGCCTGGGGCGCCCCCTGGGCTGCGGCTGCCCGGGAGACC
L P L R S G L G G A P L G L R L P R E T
GACGAAGAGCCGAGGGAGCCGGAGGGCAGCTTGAGATGGGACAACTG
D E E P E E P G R R G S F V E M V D N L
AGGGGCAAGTCGGGCAGGGCTACTACGTGGAGATGACCGTGGCAGCCCCCGAGACG
R G K S G Q G Y Y V E M T V G S P P Q T
CTCAACATCCTGGTGGATAAGGCAGCAGTAACCTTGAGCTGGGCTGCCACCC
L N I L V D T G S S N F A V G A A P H P
TTCCTGCATCGCTACTACCAGAGGCAGCTGCCAGCACATACCGGACCTCCGGAGGGC
F L H R Y Y Q R Q L S S T Y R D L R K G
GTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGAGCTGGGACCGACCTGTAAGC
V Y V P Y T Q G K W E G E L G T D L V S
ATCCCCATGGCCCCAACGTCACTGTGCGCAACATTGCTGCCATCACTGAATCAGAC
I P H G P N V T V R A N I A A I T E S D
AAGTTCTTCATCAACGGCTCCAACTGGGAAGGCATCCTGGGCTGGCTATGCTGAGATT
K F F I N G S N W E G I L G L A Y A E I
GCCAGGCCTGACGACTCCCTGGAGCCTTCTTGACTCTGGTAAAGCAGACCCAGTT
A R P D D S L E P F F D S L V K Q T H V
CCCAACCTCTTCTCCCTGCAGCTTGAGCTGGCTCCCTCAACCAGTCTGAAGTG
P N L F S L Q L C G A G F P L N Q S E V
CTGGCCTCTGTCGGAGGGAGCATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGC
L A S V G G S M I I G G I D H S L Y T G
AGTCTCTGGTATAACCCATCCGGGGAGTGGTATTATGAGGTATCATTGTGGGTG
S L W Y T P I R R E W Y Y E V I I V R V
GAGATCAATGGACAGGATCTGAAAATGGACTGCAAGGAGTACAACATATGACAAGAGCATT
E I N G Q D L K M D C K E Y N Y D K S I
GTGGACAGTGGCACCAACCTTCGTTGCCAAGAAAGTGTGAAAGCTGCAGTC
V D S G T T N L R L P K K V F E A A V K
TCCATCAAGGCAGCCTCCACGGAGAAGTCCCTGATGGTTCTGGCTAGGAGAGCAG
S I K A A S S T E K F P D G F W L G E Q
CTGGTGTGGCAAGCAGGCACCACCCCTGGAACATTTCAGTCATCTCACTCTAC
L V C W Q A G T T P W N I F P V I S L Y
CTAATGGGTGAGGTTACCAACCAGTCCTCCGCATCACCATCCTCCGCAGCAATACCTG
L M G E V T N Q S F R I T I L P Q Q Y L
CGGCCAGTGGAAAGATGTGGCACGTCCAAGACGACTGTTACAAGTTGCCATCTCACAG
R P V E D V A T S Q D D C Y K F A I S Q
TCATCCACGGGCAGTGTATGGGAGCTGTTATGGAGGGCTTCTACGTTGTCTTGAT
S S T G T V M G A V I M E G F Y V V V F D

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Fig. 6B

Phone No.: (312) 474-6300

10/18

FIGURE 6B

CGGGCCCAGAACGAATTGGCTTGCTGTCAGCGCTGCCATGTGCACGATGAGTCAGG
R A R K R I G F A V S A C H V H D E F R
ACGGCAGCGGTGGAAGGCCCTTTGTCACCTGGACATGGAAGACTGTGGCTACAACATT
T A A V E G P F V T L D M E D C G Y N I
CCACAGACAGATGAGTCATGA
P Q T D E S *

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Fig. 7A

Phone No.: (312) 474-6300

11/18

FIGURE 7A

ATGGCTAGCATGACTGGTGGACAGCAAATGGGTCGGATCGATGACTATCTCTGACTCT
M A S M T G G Q Q M G R G S M T I S D S
CCCGGTGAACAGGACGGATCCACCCAGCACGGCATCCGGCTGCCCTGCGCAGCGGCCTG
P R E Q D G S T Q H G I R L P L R S G L
GGGGCGCCCCCTGGGGCTGCGGCTGCCCGGGAGACCGACGAAGAGCCCAGGGAGCCC
G G A P L G L R L P R E T D E E P E E P
GGCCGGAGGGCAGCTTGTGGAGATGGTGGACAACCTGAGGGCAAGTCGGGCAGGGC
G R R G S F V E M V D N L R G K S G Q G
TACTACGTGGAGATGACCGTGGCAGCCCCCGCAGACGCTAACATCCTGGTGGATACA
Y Y V E M T V G S P P Q T L N I L V D T
GGCAGCAGTAACTTGCAGTGGGTGCTGCCACCCCTGCATCGCTACTACCAAG
G S S N F A V G A A P H P F L H R Y Y Q
AGGCAGCTGTCCAGCACATACCGGGACCTCCGAAGGGCGTGTATGTGCCCTACACCCAG
R Q L S S T Y R D L R K G V Y V P Y T Q
GGCAAGTGGGAAGGGAGCTGGCACCGACCTGGTAAGCATCCCCATGGCCCCAACGTC
G K W E G E L G T D L V S I P H G P N V
ACTGTGCGTGCACATTGCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCC
T V R A N I A A I T E S D K F F I N G S
AACTGGGAAGGCATCCTGGGCTGGCCTATGCTGAGATTGCCAGGCCTGACGACTCCCTG
N W E G I L G L A Y A E I A R P D D S L
GAGCCTTCTTGACTCTGGTAAAGCAGACCCACGTTCCAACCTCTCCCTGCAG
E P F F D S L V K Q T H V P N L F S L Q
CTTGTTGGCTGGCTCCCTCAACAGTCTGAAGTGCTGGCTCTGCGAGGGAGC
L C G A G F P L N Q S E V L A S V G G S
ATGATCATTGGAGGTATCGACCACTCGCTGTACACAGGCAGTCTGGTATAACACCCATC
M I I G G I D H S L Y T G S L W Y T P I
CGGCAGGGAGTGGTATTATGAGGTACATTGTCGGGGGGAGATCAATGGACAGGATCTG
R R E W Y Y E V I I V R V E I N G Q D L
AAAATGGACTGCAAGGAGTACAACATGACAAGAGCATTGGACAGTGGCACCAAC
K M D C K E Y N Y D K S I V D S G T T N
CTTCGTTGCCAAGAAAGTGGTGAAGCTGCAGTCACCATCAAGGCAGCCTCC
L R L P K K V F E A A V K S I K A A S S
ACGGAGAAGTCCCTGATGGTTCTGGCTAGGAGAGCAGCTGGTGTGGCAAGCAGGC
T E K F P D G F W L G E Q L V C W Q A G
ACCACCCCTGGAACATTTCCAGTCATCTCACTCACCTAACCTGGGAGGTTACCAAC
T T P W N I F P V I S L Y L M G E V T N
CAGTCCTCCGCATCACCATCCTCCAGCAATACCTGCAGGCCAGTGGAAAGATGTGGCC
Q S F R I T I L P Q Q Y L R P V E D V A
ACGTCCCAAGACGACTGTTACAAGTTGCCATCTCACAGTCATCCACGGGCACTGTTATG
T S Q D D C Y K F A I S Q S S T G T V M

Inventors: Gurney et al.
Title: "Alzheimer's Disease Secretase, APP Substrates
Therefor, and Uses Therefor"
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Phone No.: (312) 474-6300

Fig. 7B
12/18

FIGURE 7B

GGAGCTGTTATCATGGAGGGCTTCTACGTTGTCTTGATCGGGCCCGAAACGAATTGGC
G A V I M E G F Y V V F D R A R K R I G
TTTGCTGTCAGCGCTTGCATGTGCACGATGAGTTCAGGACGGCAGCGGTGGAAGGCCCT
F A V S A C H V H D E F R T A A V E G P
TTTGTACACCTTGGACATGGAAGACTGTGGCTACAACATTCCACAGACAGATGAGTCATGA
F V T L D M E D C G Y N I P Q T D E S *

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Fig. 8A

13/18

FIGURE 8A

ATGACTCAGCATGGTATTCTGCTGCCACTGCGTAGCGGTCTGGGTGGTCTCCACTGGGT
M T Q H G I R L P L R S G L G G A P L G -
CTGCGTCTGCCCGGGAGACCGACGAAGAGCCCAGGGAGCCCGGAGGGGAGCTTT
L R L P R E T D E E P E E P G R R G S F -
GTGGAGATGGTGGACAACCTGAGGGCAAGTCGGGCAGGGCTACTACGTGGAGATGACC
V E M V D N L R G K S G Q G Y Y V E M T -
GTGGGAGCCCCCGCAGACGCTAACATCCTGGTGGATACAGGCAGCAGTAACCTTGCA
V G S P P Q T L N I L V D T G S S N F A -
GTGGGTGCTGCCCGGACCCCTTCCTGCATCGCTACTACCAGAGGCAGCTGTCCAGCACA
V G A A P H P F L H R Y Y Q R Q L S S T -
TACCGGGACCTCCGGAAGGGCGTGTATGTGCCCTACACCCAGGGCAAGTGGGAAGGGGAG
Y R D L R K G V Y V P Y T Q G K W E G E -
CTGGGCACCGACCTGGTAAGCATCCCCATGGCCCCAACGTCACTGTGCGTGCCAACATT
L G T D L V S I P H G P N V T V R A N I -
GCTGCCATCACTGAATCAGACAAGTTCTTCATCAACGGCTCCAACGGAAAGGCATCCTG
A A I T E S D K F F I N G S N W E G I L -
GGGCTGGCTATGCTGAGATTGCCAGGCCTGACGACTCCCTGGAGCCTTCTTGACTCT
G L A Y A E I A R P D D S L E P F F D S
CTGGTAAAGCAGACCCACGTTCCCAACCTCTCCCTGCAGCTTGTGGTGTGGCTTC
L V K Q T H V P N L F S L Q L C G A G F -
CCCCTCAACCAGTCTGAAGTGCTGGCCTCTGCGGAGGGAGCATGATCATGGAGGTATC
P L N Q S E V L A S V G G S M I I G G I -
GACCACTCGCTGTACACAGGCAGTCTCTGGTATAACACCCATCCGGGGAGTGGTATTAT
D H S L Y T G S L W Y T P I R R E W Y Y -
GAGGTCAATTGTGCGGGTGGAGATCAATGGACAGGATCTGAAATGGACTGCAAGGAG
E V I I V R V E I N G Q D L K M D C K E
TACAACATGACAAGAGCATTGTGGACAGTGGCACCACCAACCTCGTTGCCAAGAAA
Y N Y D K S I V D S G T T N L R L P K K -
GTGTTGAAGCTGCAGTCAAATCCATCAAGGCAGCCTCCACGGAGAAGTTCCCTGAT
V F E A A V K S I K A A S S T E K F P D -
GGTTCTGGCTAGGAGAGCAGCTGGTGTGGCAAGCAGGCACCACCCCTGGAACATT
G F W L G E Q L V C W Q A G T T P W N I -
TTCCCACTCTCACTCTAACCTAATGGGTGAGGTTACCAACCAGTCCTTCGCATCACC
F P V I S L Y L M G E V T N Q S F R I T -
ATCCTTCCGCAGCAATACTGGCCAGTGGAAAGATGTGGCCACGTCCCAAGACGACTGT
I L P Q Q Y L R P V E D V A T S Q D D C -

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Fig. 8B

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14/18

FIGURE 8B

TACAAGTTGCCATCTCACAGTCATCCACGGGCACTGTTATGGGAGCTGTTATCATGGAG
Y K F A I S Q S S T G T V M G A V I M E -
GGCTTCTACGTTGTCTTGATCGGGCCGAAAACGAATTGGCTTGCTGTCAGCGCTTGC
G F Y V V F D R A R K R I G F A V S A C -
CATTAG
H *

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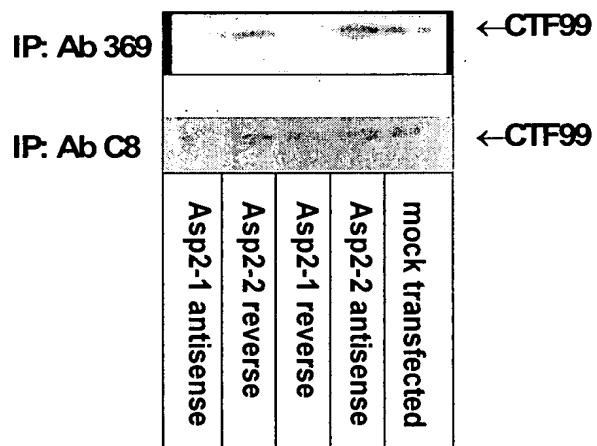
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Fig. 9

15/18

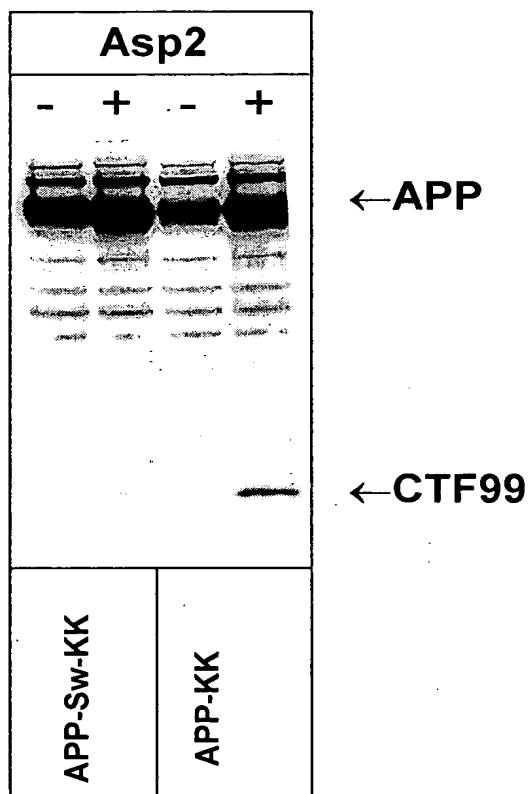
FIGURE 9



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Fig. 10
16/18

FIGURE 10



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Fig. 11
17/18

FIGURE 11

MAQALPWLLLWMGAGVLPAG TQHGIRLPLRSGLGGAPLGLRLPRETDEE
PEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFA
VGAAPHFPLHRYYQRQLSSTYRDLRKGVYVPTYQGKWEGEGLGTDLVSIPH
GPNVTVRANIAAITESDKFFINGSNWEGLGLAYAEIARPDDSLPFFDS
LVKQTHVPNLFLQLCGAGFPLNQSEVLAASVGGSMIIGGIDHSLYTGSLW
YTPIRREWYYEVIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKK
VFEAAVKSIIKAASSTEKFPGFWLGEQLVCWQAGTPWNIFPVISLYLMG
EVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVDEFRTAAVEGPFTLDMEDCGYNIPQT
DES

FIGURE 12

MAQALPWLLLWMGAGVLPAHG TQHGIRLPLRSGLGGAPLGLRLPRETDEE
PEEPGRRGSFVEMVDNLRGKSGQGYYVEMTVGSPPQTLNILVDTGSSNFA
VGAAPHFPLHRYYQRQLSSTYRDLRKGVYVPTYQGKWEGEGLGTDLVSIPH
GPNVTVRANIAAITESDKFFINGSNWEGLGLAYAEIARPDD\$LEPFFDS
LVKQTHVPNLFLQLCGAGFPLNQSEVLASVGGSMIIGGIDHSLYTGSILW
YTPIRREWYYEVIIVRVEINGQDLKMDCKEYNYDKSIVDSGTTNLRLPKK
VFEAAVKSIIKAASSTEKFPDGFWLGEQLVCWQAGTTPNIFPVVISLYLMG
EVTNQSFRITILPQQYLRPVEDVATSQDDCYKFAISQSSTGTVMGAVIME
GFYVVFDRARKRIGFAVSACHVDEFRTAAVEGPFTLDMEDCGYNIPQT
DESHHHHHH